Bandolier

What do we think?
What do we know?
What can we prove?

11

Evidence-based health care

First published January 1995

Is it worth doing?

Bandolier has panic attacks over the loose use of the word effective. Numbers-needed-to-treat (NNT [1]) is one way to define effectiveness. NNTs are easier to interpret than absolute and relative rate reduction. Two examples may help. Using flu vaccination (page 5) the reduction in relative risk was 0.42. This translates to an NNT of 23 compared with not vaccinating. One case of flu was prevented for every 23 patients vaccinated. In a powerful review of matters cardiovascular [2] the AIRE study of angiotensin converting enzyme inhibitors after myocardial infarction [3] is cited as "one of the most important clinical trials in cardiovascular medicine to be published for many years". 2006 patients with clinical evidence of heart failure were randomised to ramipril or placebo (minimum follow up six months). There were 170 deaths in the 1014 patients randomised to ramipril compared with 222 deaths in the 992 patients randomised to placebo. This relative rate reduction of 27% translates to an NNT of 18. One death was prevented for every 18 patients treated.

Both examples are of preventative interventions. It is important to appreciate that NNT is by definition context-dependent. It is flu vaccination versus no vaccination and ACE inhibitor versus placebo. The NNT would change if comparisons were different, for instance one flu vaccine versus another. For a common disorder a cheap preventative intervention with minimal adverse effects and an NNT of 50 may well be worth doing. If there are substantial adverse effects then it may not be worth doing. For a serious condition then a risk of significant adverse effects may be worth taking.

NNT makes it easy to quantify this clinical decision-making, because NNT for adverse effects can be calculated as well as NNT for effectiveness. NNT for drug-related study withdrawal in the AIRE study was 18 for ramipril compared with placebo. Like ***Bandolier***, patients may find NNT easier to understand. *"By taking this medicine you will reduce the chance of dying from your heart problem by xx; the chance of your not being able to tolerate the drug is yy"*. The next twist is to use NNTs for treatment as well as prevention.

References:

1 Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical Epidemiology: a basic science for clinical medicine. 2nd edition. Boston: Little, Brown; 1991.

2 McMurray J, Rankin A. Cardiology - I: Treatment of myocardial infarction, unstable angina, and angina pectoris. British Medical Journal 1994 309:1343-50.

3 Acute Infarction Ramipril Efficacy (AIRE) study investigators. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. Lancet 1993 342:821-8.

Screenwatch

In future months ***Bandolier*** will feature a number of pieces on screening. The Chief Medical Officer made a major speech on screening in January 1994 where he outlined the way in which screening policy and practice should be organised in future.

The approach is based on the principle that because screening is offered to healthy populations, the burden of proof of its effectiveness, the balance between beneficial and adverse effects, and the need to deliver a high quality service are all even more important in screening than in conventional clinical practice.

During 1995 it is probable that the National Screening Network will be set up as part of the Public Health Network, and it will be charged with the responsibility of ensuring that screening is better managed in future than it has been in the past. In the meantime ***Bandolier*** will carry a series of articles on screening as a regular feature.

All or none screening

The decision to screen or not to screen is an all or none decision. Either the evidence is good and the screening should be perfectly done, or it should be kept out of purchasing and clinical practice. Below is a list of screening tests that are offered in some parts of the country but for which there is insufficient evidence to support their introduction or continuation except as part of high quality research, carried out to a defined protocol with subjects informed about the experimental nature of the procedure being offered:

- screening for prostate cancer
- screening for ovarian cancer
- screening for colorectal cancer
- chlamydia screening in pregnancy
- human papilloma virus screening as part of cervical screening
- screening of neonates for congenital biliary atresia
- whole population cholesterol screening

J A Muir Gray
Director of Research and Development

BENIGN PROSTATIC HYPERPLASIA: DIAGNOSIS AND TREATMENT

The US Agency for Health Care Policy and Research (AHCPR) was established in December 1989 to enhance the quality, appropriateness, and effectiveness of health care services. From time to time AHCPR publishes evidence-based Clinical Practice Guidelines.

The eighth in the series is devoted to benign prostatic hyperplasia (BPH) diagnosis and treatment. The main book (220 pages and 300 references) is accompanied by a patient booklet and quick reference guide for clinicians. This may seem daunting, but this is a real and readable example of everything you wanted to know about BPH but were afraid to ask! ***Bandolier*** has no hesitation in encouraging any healthcare professional or patient to read and enjoy this publication.

How big is the problem?

BPH is the most common benign neoplasm (non cancerous enlargement of the prostate gland) in men, and has a high prevalence that increases with age. The increase in size of the prostate inside its capsule exerts pressure on the urethra, which passes through the capsule, resulting in obstruction to urine flow.

Half of all men have BPH identifiable histologically at age 60 years, and by 85 years the prevalence is about 90%. In the USA about 25% of men will be treated for BPH by age 80, and over 300,000 surgical procedures are performed each year for BPH (mostly transurethral resection of the prostate, TURP). This makes TURP the second most common surgical procedure, second only to cataract surgery - at a cost estimated at $2 billion per year.

What are the symptoms?

Most patients with BPH consult their GP with bothersome symptoms concerning urination. A simple symptom index has been drafted by the American Urologists Association (AUA). By answering seven questions about the severity of symptoms, it is possible to define whether the symptoms are mild (0-7 points), moderate (8-19 points) or severe (20-35 points).

This Symptom Index is recommended as the symptom scoring instrument to be used in the initial assessment of each patient presenting with symptoms of prostatism, and should be the primary determinant of treatment response or disease progression in the follow up period.

What diagnostic tests are useful?

Although there are a number of diagnostic test procedures which can be used for BPH, urine flow rate recording is the single best non invasive urodynamic test to detect lower urinary tract obstruction. There is insufficient evidence to recommend a cut-off value to document appropriateness of therapy.

This test measures the peak or average flow rate of urine, and peak flow rates (Q_{max}) of above 15 mL/second are usually found in asymptomatic men of 25 to more than 60 years of age. Responses to treatment are less good in patients with a Q_{max} of more than 15 mL/sec.

AUA Symptom Index

Circle 1 number on each line

Questions to be answered	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1: Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2: Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?	0	1	2	3	4	5
3: Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
4: Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5: Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6: Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
7: Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5

Sum of 7 circled numbers (AUA Symptom Score): _____

Other diagnostic tests such as post void residual urine volume and some pressure flow studies are regarded as optional, but other tests (filling cystometry, urethrocystoscopy, imaging of the urinary tract) are not recommended.

What are the treatment options?

There are a number of treatment options (see box). These include watchful waiting, medical therapy, balloon dilatation and various surgical procedures.

The effects of these various treatments on peak urinary flow rate have been surveyed in the AHCPR review, and are summarised in the figure. TURP and open prostatectomy, as well as TUIP (which is not commonly performed in the UK) are the most effective in producing an increase in urinary flow rate.

Similar summaries of the effects of various treatments on symptom improvement are shown in the table. About half the patients treated with placebo or watchful waiting reported symptom improvement, compared with about 90% for TURP. The proportion reporting worse symptoms is small (usually less than 5%) except for watchful waiting where it can be as high as 25%.

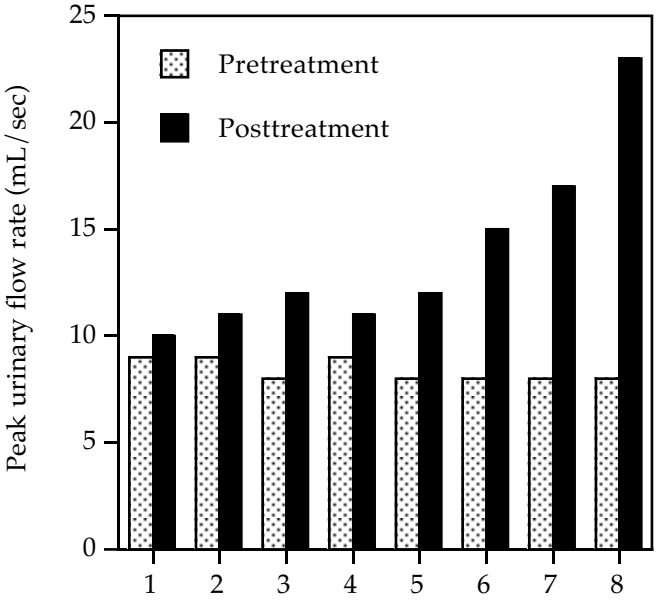
The AHCPR review has also estimated the magnitude of the symptom improvement. For the placebo and medical treatments this was of the order of 30-40% improvement, but for the surgical procedures was 70-85% improvement, clearly superior to other treatments.

Treatment	Median probability of symptom improvement (percent , 90% CI)
Placebo	45 (26 - 65)
Watchful waiting	42 (31 - 55)
Alpha blocker	74 (59 - 86)
Finasteride	67 (54 - 78)
Balloon dilation	57 (37 - 76)
TUIP	80 (78 - 83)
TURP	88 (75 - 96)
Open prostatectomy	98 (94 - 99)

What are the adverse events with treatment?

Few treatments are without any adverse consequences, and this is particularly so with treatments with BPH, where there is a delicate balancing act between the benefits and demerits of the treatments available.

Mean pre- and post treatment urinary flow rates for various BPH treatments



Treatment
1 Placebo
2 Watchful waiting
3 Alpha blocker
4 Finasteride
5 Balloon dilation
6 TUIP
7 TURP
8 Open prostatectomy

BPH Treatment Options

Watchful waiting: A strategy of management in which the patient is monitored but receives no active treatment.

Alpha blocker therapy: Treatment using alpha-1-adrenergic receptor blockers that inhibit contraction of prostatic smooth muscle.

Finasteride therapy: Treatment using finasteride, an enzyme inhibitor that lowers prostatic androgen levels and can result in some decrease of prostate size.

Balloon dilation: A catheter with a balloon at the end is inserted through the urethra and into the prostatic urethra. The balloon is then inflated to stretch the urethra where narrowed by the prostate.

Transurethral incision of the prostate (TUIP): An endoscopic surgical procedure in which patients with smaller prostates (<30 g) have an instrument inserted through the urethra to make one or two cuts in the prostate and reduce the constriction on the urethra.

Transurethral resection of the prostate (TURP): Surgical removal of the prostate's inner portion by endoscopic approach through the urethra. This is the most common active treatment.

Open prostatectomy: Surgical removal of the prostate via an incision in the lower abdomen. It usually requires a longer hospital stay.

The adverse events following treatment for BPH include impotence (with 90% confidence intervals for various surgical procedures ranging from about 4 % to 40%; the incidence of impotence is also increased after some medical treatments), incontinence (stress incontinence about 3% after surgery, with total urinary incontinence approaching 1%), and the need for re-treatment.

Re-treatment over a five year period was calculated by the AHCPR for a number of treatment options. Thus for watchful waiting, balloon dilation and medical treatments some 30-40% of men would expect to suffer treatment failure over five years; for surgical procedures treatment failure over the same period was calculated at 2-10%.

Combined analysis of published data estimated that the mean probability for perioperative mortality (death within 90 days of a procedure) was 1.5% for TURP. For open surgery it was 2.4% and for balloon dilation it was 3.5%.

What do treatments cost?

The AHCPR has calculated treatment costs from Medicare data. In absolute terms this is not entirely pertinent for British experience, but the relative costs are probably similar, and the figures are given in the table below in US$.

Treatment	Cost of first year	Cost of second year
Watchful waiting	1,162	640
Finasteride	1,326	788
Alpha blocker	1,395	845
Balloon dilation	3,723	543
TURP	8,606	360
Open prostatectomy	12,788	69

Treatment preference?

BPH affects the quality rather than the quantity of life. It is therefore the degree to which the patient's symptoms bother him that will determine the need for therapy; the relative benefits and harms of each treatment option will help to determine their therapeutic preference.

AHCPR therefore gauged the range of personal preferences by looking at the way in which a small band of patients (53) who were given information on the benefits and adverse effects of different treatments made judgements about their own treatment options. Nine of the 53 had mild symptoms, 19 moderate and 12 severe symptoms by the AUA scoring system.

The results are shown in the figure. Watchful waiting was the most frequently chosen treatment for those patients with mild and moderate symptoms. Those with severe symptoms most frequently chose surgery. Medical therapies and balloon dilation were chosen by only a small percentage of the patients.

New treatment options?

There are number of new treatment options becoming available, though none of these has yet to be tested rigorously in randomised controlled trials, and even in the open studies so far reported there is no clear indication that they offer any particular benefits over conventional therapies. Judgement, however, must await publication of good clinical trials.

The new therapies fall into some clear groups.

Laser prostatectomy uses energy from directed neodynium yttrium aluminium garnet lasers to destroy prostate tissue. Initially bare laser fibres were used, with fairly disappointing results, but later technology advances enabled right angled fibres to direct the laser energy more directly at the tissue. The lasers are directed by ultrasound or direct cystoscopy.

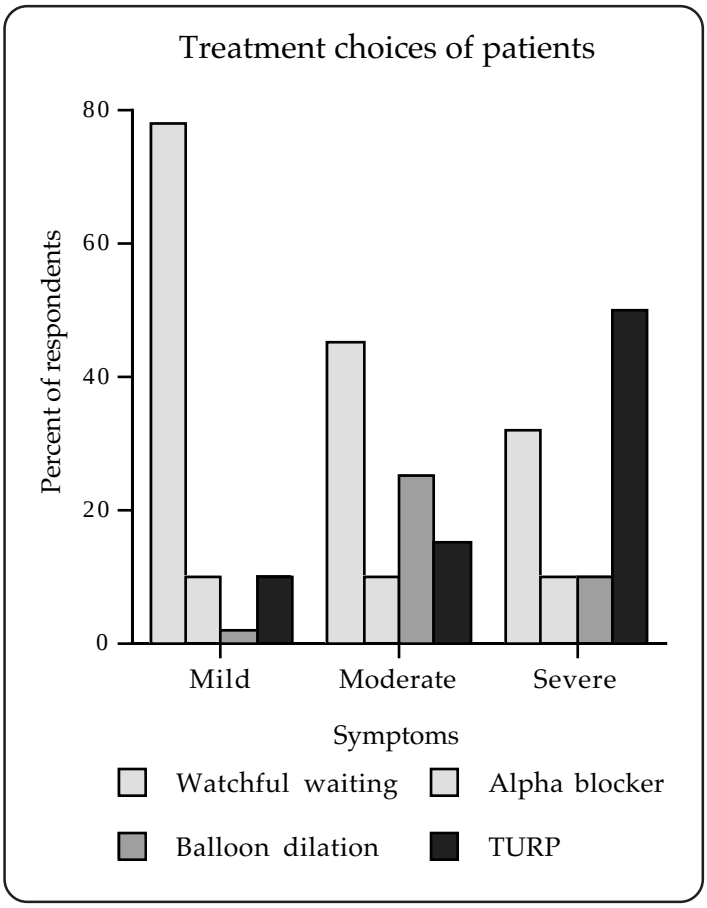
Hyperthermia of the prostate tissue utilises microwaves to 'cook' the prostate tissue and destroy it. A number of technologies have been used to deliver microwaves transrectally or transurethrally.

Prostatic stents are metal devices that can be placed in the prostatic urethra to expand the urethra and make urine flow easier.

To these surgical options must be added a number of medical treatments currently under trial. The AHCPR report concluded that there was presently insufficient data on any of these to permit conclusions regarding their safety and efficacy. The new treatments should not form part of purchasing contracts until one year follow up data from properly conducted randomised controlled trials are available.

How to get the report

Copies of this highly recommended report and the associated documents are available from AHCPR Publications Clearinghouse, PO Box 8574, Silver Spring, MD 20907-8547, USA (Tel 001-800-358-9295).



COCHRANE CORNER

Update on the Cochrane Collaboration

The Cochrane Collaboration was launched in October 1993, and so is just emerging from infancy and developing into toddlerhood. The Collaboration is a network of individuals, and its objectives are to prepare, maintain and disseminate systematic reviews of the effects of health care. This is a huge challenge. To illustrate just how huge, achieving even the first of these objectives will take a considerable time, as it can take up to five years to prepare a proper systematic review. Currently there are no Cochrane reviews available for dissemination, but the first will appear early in 1995.

The added value of a Cochrane review (as opposed to any other systematic review) is the commitment to regular updating. Reviews published in journals are often out of date by the time they are published. Cochrane reviews will be published electronically and updated when this is appropriate. They will therefore be dynamic and changing to take into account new evidence as soon as it is available.

Each Cochrane reviewer is a member of a Collaborative Review Group (CRG), which consists of people who share an interest in a particular topic (for example, stroke, diabetes, incontinence, or oral health). The CRGs focus on health problems. Other dimensions of interest (such as primary health care, developing countries, care of the elderly, or alternative medicine) are addressed through Field Co-ordination. The work of the CRGs and the Fields is facilitated in a variety of ways by the various Cochrane centres.

1,000 people involved

More than 1,000 people from over 50 countries are either already contributing to the work of the Collaboration, or have indicated their desire to contribute. Throughout the Collaboration, about 40 CRGs and 15 Fields are in various stages of evolution. Sixteen CRGs have registered with the Collaboration, and even these 16 reflect a great diversity. They include, for example, parasitic diseases, osteoporosis, back pain, subfertility and schizophrenia.

Around the world there are seven Cochrane centres established so far, and several others in various stages of development. Each centre has general responsibilities, such as helping to maintain a directory of contributors to the Collaboration, maintaining registers of systematic reviews, and helping to establish a register of all randomised controlled trials. In addition, the centres all have particular interests, which include methodological research, dissemination of information useful for delivery of appropriate health care, and consumer involvement in the process of reviewing.

Lelia Duley

Anyone in the UK interested in contributing should contact:
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INFLUENZA VACCINATION IN THE ELDERLY

Most of the deaths due to influenza occur among people aged over 60 years of age. It is in this group, and others with particular medical disorders (heart or lung disorders, diabetes, chronic renal insufficiency or chronic staphylococcal infections), that influenza vaccination is recommended. The question of how effective the vaccination policy is in elderly persons has been answered by a randomised controlled trial published recently in the Journal of the American Medical association [1].

The study was conducted in the winter of 1991-2 in southern Holland. Nearly 10,000 people not known to be belonging to a high-risk group in 15 practices were asked whether they wished to take part in the study and just under 2,000 accepted.

Randomised controlled trial

People were randomly allocated to active vaccine or control, which were given in double-blind conditions in weeks 44-46 (November 1-16). The active vaccine consisted of two Beijing strains, a Singapore and a Panama strain.

Participants gave blood samples before vaccination, three weeks later, and five months later for serological testing for increased antibody levels. The participants and their GPs also completed forms relating to any symptoms of influenza according to defined protocols.

The vaccination occurred before a peak of influenza incidence in Holland, during three weeks at the end of 1991.

Results

In the vaccinated population the rate of influenza or influenza-like illness was half that in the vaccinated population compared with the population given a placebo vaccination. For influenza confirmed both clinically and serologically, the relative risk was 0.42 (CI 0.23 to 0.74).

Using the more user-friendly numbers-needed-to-treat (NNT) method of calculating the results, of about two cases of influenza expected each winter in every 23 people aged over 60 years, one was prevented by influenza vaccination. Preventing one case of influenza for every 23 people treated, and preventing half the cases in elderly people is a very positive result, and one which should encourage the active pursuit of the policy of influenza vaccination.

Conclusion

With the JAMA paper is a very thoughtful editorial [2]. As well as commenting generally on the need for RCTs, and on the effectiveness of this RCT in particular, it reviews much up-to-date literature on the effectiveness of influenza vaccination. It refers to several studies in which substantial savings were demonstrated in direct medical costs during successive influenza seasons among elderly people who had been vaccinated.

The editorial delivers a simple message, based on the RCT and other evidence. "Influenza vaccination works, it's inexpensive, and it saves money".

References

1 ME Govaert, CTMNC Thijs, N Masurei, MJW Sprenger, GJ Dinant, JA Knottnerus. The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial. Journal of the American Medical Association 1994 272:1661-5.

2 PA Patriarca. A randomised controlled trial of influenza vaccine in the elderly. Scientific scrutiny and ethical responsibility. Journal of the American Medical Association 1994 272:1700-1.

GUIDELINES

The eighth Effective Health Care bulletin was published in December, with the title "Implementing Clinical Practice Guidelines". The bulletins are based on a systematic review and synthesis of the literature on the clinical effectiveness, cost effectiveness and acceptability of health service interventions. The review and synthesis of the literature is carried out by a research team using established methodological checklists, with advice from expert consultants. ***Bandolier*** has reviewed previously several of the Effective Health Care bulletins.

Clinical Practice Guidelines

There is increasing interest in the potential of clinical practice guidelines to promote the effectiveness and efficiency of health care. The NHS Executive has recommended that guidelines should be used to 'inform contracts'.

This bulletin examines the evidence on whether practice guidelines can change the behaviour of health professionals and, if so, how best to introduce them into clinical practice. The bulletin also considers the characteristics of high quality guidelines and how purchasers might use guidelines for commissioning.

The authors have assembled together a prodigious amount of information; there are 150 references and several pages of comprehensive tables which assemble the evidence from rigorous studies of guideline introduction.

The bulletin is tightly written but easily digested. It provides an easy access to evidence based information about guidelines for any individual or group working on guideline introductions. The main points from the bulletin are:

Implementing Clinical Practice Guidelines: Main Recommendations

- Practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.

- The introduction of guidelines can change clinical practice and affect patient outcome. The ways in which guidelines are developed, implemented and monitored influence the likelihood of adherence.

- Guidelines are more likely to be effective if they take into account local circumstances, are disseminated by an active educational intervention, and implemented by specific reminders relating directly to professional activity.

- Guidelines should be firmly based on reliable evidence of clinical and cost effectiveness. Recommendations should be explicitly linked to the evidence. Few national or local guidelines are sufficiently based on evidence.

- National initiatives are needed to help provide the evidence base which can be incorporated into national and local guidelines.

- Priority should be given to the development and introduction of local guidelines where nationally produced rigorous guidelines exist or where the evidence base is readily available. Priority should be given to areas where current practice diverges from best practice providing the potential for significant gains in health.

- A coherent programme of research is needed to ensure that guidelines are used to their full potential.

Copies of previous bulletins are available at £3 each. Those published are:

1: Screening for osteoporosis to prevent fractures.
2: Stroke rehabilitation.
3: The management of subfertility.
4: The treatment of persistent glue ear in children.
5: The treatment of depression in primary care.
6: Cholesterol: Screening and Treatment.
7: Brief Interventions and Alcohol use.
8: Implementing Clinical Practice Guidelines.

Payment by cheque payable to 'University of Leeds', and orders should be sent to Effective Health Care, 71-5 Clarendon Road, Leeds LS2 9PL.

A Practical Guide to Fundholding - Book Review

This book is written by enthusiasts who have been in fundholding since its inception. Its authors are two GPs, two fund managers and the regional primary care manager for the (old) Oxford RHA. It has an inevitable regional bias, but this is also a strength as the authors use much illustrative information from regional statistics which better illuminate the subject.

The book is unashamedly practical in its outlook, aiming to assist GPs and members of the primary health care team who are new to fundholding. It covers each aspect of the procedure, from the important preparatory year through negotiating budgets and contracts (with illustrative examples), managing the funds, monitoring, fundholders working together and aspects of the future of fundholding. It is a step-by-step walk through the fundholding maze with experienced guides.

To take one example: the section on negotiating contracts includes how to conduct the negotiations themselves, and the subsection on negotiating tactics is a classic description of the way in which negotiations work in any arena and is a worthwhile read for anyone engaged frequently or infrequently in complex negotiations.

The foreword by Virginia Bottomley ventures that the book will help those who have decided to join the fundholding scheme, and she is right.

"A Practical Guide to Fundholding" is written by Rod Smith, Shaun Brogan, Richard Stephenson, Janet Fitzgerald and Lesley Withers (ISBN 0-632-03869-1). It is published by Blackwell Science Limited, and distributed in the UK by Marston Book Services, PO Box 87, Oxford OX2 0DT (Tel 01865 791155, Fax 01865 791927).

Desert Island Texts

When I started thinking about what books I would like to have with me on a desert island the three that have most influenced me came to mind. The common denominator amongst them is that they are about how social systems work. All of them are from outside the health sector, but that is all to the good. We need to understand that behaviours in health care are not unlike those in other sectors and equally we need to understand the wider environment in which we work.

"Diffusions of Innovations"

E M Rogers wrote the book with this title. It sounds a bit dry but in part it offers enormous insight into the way change takes place in any social system: the path that is followed, the types of change which will be easy to make and those which will be difficult. It makes so clear that the health system is no different from others. However, it is an academic work summarising 7,400 individual studies and in my lonely existence on a desert island I felt it wasn't quite warm enough to be the one book I was left with.

"Essence of Decisions"

This book by Graham Allison is about the Cuban Missile Crisis and the game of chess which was being played between the USA and USSR at the time. It looks at the events from three alternate decision making paradigms. It made me realise that how we operate will depend so much on our own preferred mode, for example how much is it about logic or alternatively how much we intuitively think through how someone else will react, but also how we are influenced by the way a particular organisation does things.

"Age of Unreason"

The book I finally decided I would want with me is Charles Handy's "The Age of Unreason". If you are at all interested in what is happening in organisations and in the wider economic environment in the 1990's, this is an essential read.

Charles Handy doesn't necessarily explain why things are happening as they are, but he certainly puts our world in a wider context. It often seems ridiculous to me that those in the NHS are working so hard with such long hours when there are so many people unemployed. Handy shows that this phenomenon applies in organisations across all the developed world. If we are going to make society in the next century at all comfortable to live in we need to understand what is happening and take steps to change our societal approach.

That would give me plenty to think about on my desert island and perhaps result in some new thinking I could bring back into the real world - following my rescue!

Barbara Stocking
Anglia & Oxford Regional Health Authority

The consumer's guide to subgroup analysis

The Annals of Internal Medicine carried a very important article in 1992 on "the extent to which a clinician should believe and act on the results of subgroup analyses of data from randomised controlled trials or meta-analyses". The authors pointed out that the extent was controversial and they provided guidelines for making decisions about the validity and relevance of subgroup analysis.

In classic McMaster style they gave a simple table of guidelines. The article is set out so that each of the questions in the box is answered and there is a very useful list of references at the end. Anyone working with clinicians and trying to encourage clinicians to make better use of trial and meta-analysis data would be well advised to read this excellent paper.

Guidelines for deciding whether apparent differences in subgroup response are real

1 Is the magnitude of the difference clinically important?
2 Was the difference statistically significant?
3 Did the hypothesis precede rather than follow the analysis?
4 Was the subgroup analysis one of a small number of hypotheses tested?
5 Was the difference suggested by comparisons within rather than between studies?
6 Was the difference consistent across studies?
7 Is there direct evidence that supports the hypothesised difference?

Reference:

AD Oxman, GH Guyatt. Annals of Internal Medicine 1992 116:78-84.